## REMARKS

Claims 12- 33 are pending. Applicants have cancelled claims 19-20, and 31-33. Applicants have amended the specification to remove cross-reference to U.S. Patent No. 5,834,247 and have amended claims 12, 14-17, 22, 24, 25 and 28-30. No new subject matter has been added. Applicants thank Examiner Moore and Supervisory Examiner Dr. Achatamurphy for the opportunity of discussing the claims in an interview on August 15, 2003.

Support for the addition of the term " 2-mercaptoethanesulfonic acid" can be found, for example, in the description of Figure 2 on page 4 or page 8 of the description and further was present in dependent claims now canceled. Support for "chitin binding domain" (CBD) is found in the description of Figure 1 on page 4. Support for "synthetic peptide or protein" can be found on page 8, line 9.

The Examiner has rejected the claims under the judicially created doctrine of double patenting with respect to U.S. Application Serial No. 09/249,543 (filing date February 12, 19992) based on U.S. Provisional Application Serial No. 60/102,413 filed September 30, 19989. The International Filing Date (PCT Publication No. WO/18881) of the present U.S. National Application is September 30, 1999 based on the U.S. Provisional Application Serial No. 60/102,413. Applicants respectfully submit that the subject matter claimed in the present claims as now amended is patentably distinct from the subject matter in the co-pending Application and that the double patenting rejection should be reversed.

**Rejections under 35 U.S.C. §102**

Claims 12-14, 16, 25 and 27 are for the reasons of record rejected under 35 U.S.C. §102(e) as being anticipated by Comb, et al. U.S. Patent No. 5,834,247, of record.

The present amended claims all require the use of 2-mercaptoethanesulfonic acid as the thiol reagent for improved cleavage of the intein, intein derivative or mutant intein. This requirement is neither suggested nor taught in Comb et al. Applicants request that the rejection under 35 U.S.C. §102(e) be reversed.

Claims 12-14, 17-19, 25 and 26 are for reasons of record rejected under 35 U.S.C. §102(b) as being anticipated by Chong, et al., *Gene*, 192:271-281 (1997), of record.

Chong et al. describes purification of proteins not the intein dependent joining of two proteins or a protein and a peptide. Moreover, Chong et al. neither suggests nor teaches the use of 2-mercaptoethanesulfonic acid as a thiol reagent which is a requirement of the present amended claims. Consequently, Applicants respectfully submit that the present rejection be reversed. Chong et al. do not teach the linker sequences now required in claims 17 and 18.

Claims 12-14, 17-19, 22, 25 and 26 are rejected under 35 U.S.C. §102(a) as being anticipated by Severinov, et al., *The Journal of Biological Chemistry* 273:16205-16209 (1998), of record.

Severinov et al describe protein ligation using the vectors supplied by New England Biolabs, Inc. to express fusion proteins for purposes of studying transcription. (see Methods on page 16205). The reference teaches the use of thiophenol as a thiol reagent. It does not teach or suggest the use of 2-mercaptoethanesulfonic acid as a thiol reagent nor the use of linkers required in claim 17.

Claims 12-14, 17, 18, 22, 25 and 26 are rejected under 35 U.S.C. §102(a) as being anticipated by Muir, et al., 1998, of record.

Muir et al. describe the use of New England Biolab, Inc. vectors containing inteins and a protein binding domain for preparing precursor proteins for cleavage and protein ligation. The reference utilizes thiophenol but neither suggests or teaches the use of 2-mercaptoethanesulfonic acid as a thiol reagent nor the use of linkers specified in claim 17.

**Rejection under 35 U.S.C. §103**

This Application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the Examiner correctly presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein.

Claims 15, 17, 18, 23 and 24 are rejected under 35 U.S.C. §103(a) as obvious over Comb, et al. as applied to claims 12-14, 16, 17 above, in view of Chong, et al., 1997, discussed above with reference to claims 12-14, 17 and 18, and Severinov, et al., discussed above with reference to claims 12-14, 17-19 and 22.

The present claims define an improved method for obtaining a protein having a C-terminal thioester for ligating to a synthetic peptide or protein having an N-terminal cysteine. The improvement resides in the identification of an improved thiol reagent. Claim 17 specifies linkers in the plasmid for expressing protein. As discussed above, Comb et al., Chong et al. and Severinov, et al. do not suggest or teach the improved thiol reagent or the specified linkers and therefore these references cannot be properly combined to suggest the present claimed invention.

Claims 12-14 and 17-19 are for reasons of record rejected under 35 U.S.C. §103(a) as being anticipated by Chong, et al., 1997, as applied to claims 12-14 and 17-19 above, in view of Telenti, et al., 1997, of record.

Chong et al. has been discussed above. Telenti describes a single example of an intein, the Mxe GyrA intein, which is characterized in the reference with respect to splicing and cleavage but not with respect to its use in ligation with a particular thiol reagent or linkers. Consequently, Applicants submit that the combination of Chong et al. and Telenti et al. do not suggest or teach the present claimed invention.

## CONCLUSION

For the reasons set forth above, Applicants respectfully submit that the rejections set forth in the Official Action of May 23, 2003 have been overcome and that this case is in condition for immediate allowance. Early and favorable consideration leading to prompt issuance of this Application is earnestly solicited.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned Attorney would appreciate the opportunity to do so. Thus, the Examiner is hereby authorized to call the undersigned collect at the number shown below.

Respectfully submitted,

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